UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/669,033	09/25/2000	Roderic M K Dale	OLIG-017CON	5652

7590 12/19/2001

Diane L Devore
Bozicevic Field & Francis LLP
285 Hamilton Avenue Suite 200
Palo Alto, CA 94301

EXAMINER
KIM, YOUNG J

ART UNIT	PAPER NUMBER
1631	5

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/669,033	Applicant(s) DALE, RODERIC M K	
	Examiner Young J. Kim	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 6-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Preliminary Remarks

Applicants are reminded that the Preliminary Amendment received on September 25, 2000, adding claims 6-14, contained error in claim numbering. The application as originally filed contained claims 1-8, of which claims 1-5 have been cancelled. Therefore, the application already contained claims 6-8. Therefore, the new claims added by the Applicants have been renumbered to 9-17 in accordance with 37 CFR 1.126.

Claims 6-17 are pending.

Specification

The specification is objected to for containing a misspelled word, "preferab;y" on line 11, pp. 25. Appropriate correction is required.

The specification is objected to because on page 40, line 6, terms "SEQ ID NO: 1" and "SEQ ID NO: 2" are recited. However, the there appear to be no nucleic acid sequences that are associated with the SEQ ID Numbers, nor does the application have a separate paper copy of the Sequence Listing, or a CRF (computer readable format) containing these sequences. It appears that the terms are borrowed from the disclosure of the cited reference (L.L. Cummins et al.). Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham et al. (US Patent No. 6,127,120, issued October 3, 2000, 102(e) date April 21, 1998) in view of Cook et al. (US Patent No. 6,127,533, issued October 3, 2000, priority date February 14, 1997) and Fodor et al. (US Patent No. 5,800,992, issued September 1, 1998, priority date March 7, 1990).

The claims are drawn to a method of identifying nucleotide difference between the sequence of a target nucleic acid and a reference nucleic acid. The difference in the sequences are determined by using a reusable array (or a substrate comprising probes) of modified probes wherein the first target nucleic acids are hybridized/detected, followed by removal of the hybridized target nucleic acids (i.e., stripping the array), and a subsequent hybridization of the reference nucleic acids the their detection. Some embodiments are drawn to the properties of the arrayed probes.

Graham et al. discloses a modified polynucleotide probe which "inhibit enzyme degradation while its remaining internucleotide linkages...maintain duplex stability (stable hybridization complex)" (column 20, lines 1-5). Graham et al. also discloses that the stage for mounting the sample could be designed to accommodate one or more of the following solid supports, such as silicon wafer, chip, higher density array microwell plate, or a membrane (column 26, lines 19-24). Graham explicitly teaches the modified probes could be plated out on an oligonucleotide array hybridized with mRNA and their hybridization pattern analyzed, followed by treatment with an RNAse or alkali for reuse of the array (column 31, lines 60-66).

Graham et al. does not disclose the probes having higher binding affinity to their complements.

Graham et al. does not specifically teach that the reusable array could be used to compare a target nucleic acid sequence to a reference sequence.

Cook et al. discloses an oligonucleotide of 15 to 50 bases in length (column 5, lines 25-30) that exhibit hybridization properties of higher quality relative to wild-type DNA-DNA and RNA-DNA duplexes (column 7, lines 16-19).

Fodor et al. discloses a reusable array for comparing the hybridization pattern of a target sequence to a reference sequence (column 3, lines 20-30). Fodor et al. also discloses that after a particular sequence has been hybridized (i.e., target sequence) and the pattern of the hybridization analyzed, the matrix substrate should be reusable and readily prepared for exposure to a second or subsequent target polynucleotides (column 25, lines 4-8) wherein the array is prepared for reuse by treatment with "various detergents or solvents to which the substrate, the oligonucleotide probes, and the linkages to the substrate are inert....includ[ing] elevated temperature treatment, treatment with organic or inorganic solvents, modifications in pH, and other means for disrupting specific interactions" (column 25, lines 9-15).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Graham et al., Cook et al., and Fodor et al. to arrive at the invention as claimed. One of ordinary skill in the art would have been motivated to combine the teachings because by doing so, one of ordinary skill in the art would have been able to form a stable hybrid-complex between the probes and their targets, thereby enabling more stringent wash conditions for more accurate detection. One of ordinary skill in the art would have been

further motivated to combine the method taught by Fodor et al., that is, comparing a target nucleic acid to a reference nucleic acid by use of a mircroarray that is reusable, wherein the array's reusability is effected "by other means for disrupting specific interactions" (Fodor et al., column 25, line 15) between the probe and its complement nucleic acid, with the teachings of Graham et al., wherein the "other means" of reusability are provided.

Although neither of the artisans specifically discloses the degree of affinity or the degree of stability/resistance as the claims recite, the artisans do disclose such properties. Since the PTO does not have the facility to conduct experiment, absent evidence to the contrary, it is determined that the degree of affinity and the stability/resistance is within the degree claimed.

Therefore, the invention as claimed obvious over the cited references.

Claims 9-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graham et al. (US Patent No. 6,127,120, issued October 3, 2000, 102(e) date April 21, 1998) in view of Cook et al. (US Patent No. 6,127,533, issued October 3, 2000, priority date February 14, 1997), Hacia et al. (US Patent No. 6,013,449, issued January 11, 2000, filed November 26, 1997), McGall et al. (US Patent No. 6,156,501, issued December 5, 2000, priority October 26, 1993), and Fodor et al. (US Patent No. 5,800,992, issued September 1, 1998, priority date March 7, 1990).

The claims are drawn to a method of identifying nucleotide difference between the sequence of a target nucleic acid and a reference nucleic acid. The difference in the sequences are determined by using a reusable array (or a substrate comprising probes) of modified probes wherein the first target nucleic acids are hybridized/detected, followed by removal of the hybridized target nucleic acids (i.e., stripping the array), and a subsequent hybridization of the

reference nucleic acids the their detection. Some embodiments are drawn to the physical properties of the arrayed probes. Some embodiments are drawn to differential labeling of the reference and the target nucleic acids.

Graham et al. discloses a modified polynucleotide probe which "inhibit enzyme degradation while its remaining internucleotide linkages...maintain duplex stability (stable hybridization complex) (column 20, lines 1-5). Graham et al. also discloses that the stage for mounting the sample could be designed to accommodate one or more of the following solid supports, such as silicon wafer, chip, higher density array microwell plate, or a membrane (column 26, lines 19-24). Graham explicitly teaches the modified probes could be plated out on an oligonucleotide array hybridized with mRNA and their hybridization pattern analyzed, followed by treatment with an RNAse or alkali for reuse of the array (column 31, lines 60-66).

Graham et al. does not disclose the probes having higher binding affinity to their complements.

Graham et al. does not disclose the differential labeling of the reference and target nucleic acids.

Graham et al. does not specifically teach that the reusable array could be used to compare a target nucleic acid sequence to a reference sequence.

Graham et al. does not disclose the use of acidic conditions for removing hybridized nucleic acids from the arrayed probes.

Cook et al. discloses an oligonucleotide of 15 to 50 bases in length (column 5, lines 25-30) that exhibit hybridization properties of higher quality relative to wild-type DNA-DNA and RNA-DNA duplexes (column 7, lines 16-19).

Hacia et al. discloses the two-color labeling scheme of a wild type fluorescein-labeled ("green") reference and biotinylated (stained with phycoerythrinstreptavidin "red" conjugate after hybridization) RNA test targets (column 13, lines 34-40).

Fodor et al. discloses a reusable array for comparing the hybridization pattern of a target sequence to a reference sequence (column 3, lines 20-30). Fodor et al. also discloses that after a particular sequence has been hybridized (i.e., target sequence) and the pattern of the hybridization analyzed, the matrix substrate should be reusable and readily prepared for exposure to a second or subsequent target polynucleotides (column 25, lines 4-8) wherein the array is prepared for reuse by treatment with "various detergents or solvents to which the substrate, the oligonucleotide probes, and the linkages to the substrate are inert....includ[ing] elevated temperature treatment, treatment with organic or inorganic solvents, modifications in pH, and other means for disrupting specific interactions" (column 25, lines 9-15).

McGall et al. discloses an array of modified oligonucleotides probes, wherein the modification comprise 7-deazaadenine and 7-deaazaguanine, in order to stabilize the oligonucleotide probes towards acidic conditions (column 9, lines 47-50) wherein such property could be useful for either the "fabrication or subsequent use (or reuse) of the arrays" (column 9, lines 37-39).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Graham et al., McGall et al., Cook et al., Hacia et al. and Fodor et al. to arrive at the invention as claimed. One of ordinary skill in the art would have been motivated to combine the teachings because by doing so, one of ordinary skill in the art would have been able to form a stable hybrid-complex between the probes and their targets,

thereby enabling more stringent wash conditions for more accurate detection. One of ordinary skill in the art would have been further motivated to combine the differential labeling scheme of Hacia et al. with the method taught by Fodor et al., that is, comparing a target nucleic acid to a reference nucleic acid (via differential labeling) by use of a mircroarray that is reusable, wherein the array's reusability is effected "by other means for disrupting specific interactions" (Fodor et al., column 25, line 15) between the probe and its complement nucleic acid, with the teachings of Graham et al. and McGall et al., wherein the "other means" of reusability are provided.

Therefore, the invention as claimed is obvious over the cited references.

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028. Papers related to this application may be submitted to Art Unit 1631by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

12/11/01

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600